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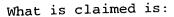
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A hapten-carrier conjugate comprising the structure shown in
 Figure 1b, wherein A, B, C, D, E, and F are branches off the tropane ring, and are each selected from the group of chemical moieties identified by CJ reference number, consisting of:

	CJ 0	 Q
10	сј 1	(CH ₂) _n Q
	CJ 1.1	co ₂ Q .
	CJ 1.2	COÕ
15	CJ 1.3	OCH ₃
	CJ 2	OCO(CH ₂) _n Q
	CJ 2.1	OCOCH=Q
	CJ 2.2	OCOCH(O)CH ₂
	CJ 2.3	OCO(CH ₂) CH(O)CH ₂
	CJ 3	CO(CH ₂) COQ
20	CJ 3.1	CO(CH ₂) CNQ
	CJ 4	$OCO(CH_2) COQ$
	CJ 4.1	OCO (CH ₂) CNQ
	CJ 5	$CH_2OCO(CH_2)_nCOQ$
	CJ 5.1	CH ₂ OCO (CH ₂) CNQ
25	СЈ 6	CONH (CH ₂) Q
	СЈ 7	Y(CH ₂) _n Q
	CJ 7.1	CH ₂ Y(CH ₂) _n Q
	CJ 8	OCOCH (OH) CH ₂ Q
	CJ 8.1	OCO (CH ₂) CH (OH) CH ₂ Q
30	CJ 9	ococ H 5
	CJ 10	See Figure 2b
	CJ 11	YCO(CH ₂) COQ

wherein Y is sulfur (S), oxygen (O), or an amine (NH), wherein n is an integer from 3 to 20, and wherein Q is selected from the group consisting of: H, OH, OCH3, CH2, CH3, COOH, halogens, activated esters, mixed anhydrides, acyl halides, acyl azides, alkyl halides, N-maleimides, imino esters, isocyanate,

The second secon

s carrier, is referred to herein as the hapten.

115 isothiocyanate, and a T cell epitope-containing carriers the proviso that Q in at least one of A, B, C, D, E, or F comprises at least one T cell epitope containing carrier, and the conjugate, with the exception of the T cell epitope-containing

- The hapten-carrier conjugate of claim 1 wherein at least one hapten is coupled to the carrier.
- The hapten-carrier conjugate of claim 2 wherein at least two 10 3. haptens are coupled to the carrier, and the haptens are the same.
 - The hapten-carrier conjugate of claim 2 wherein the carrier is multivalent.
- The conjugate of claim 1 wherein the T cell epitope-5. containing carrier is selected from the group consisting of a T cell epitope-containing protein, a modified T cell epitopecontaining protein, a T cell epitope-containing peptide, a 20 modified T cell epitope-containing peptide, a T cell epitopecontaining peptidomimetic, T cell epitope-containing multiantigenic peptides (MAP), and at least one of the chemical moieties being identified by the CJ reference number and comprising at least one T cell epitope.
- The conjugate of claim 5 wherein the T cell epitopecontaining carrier is selected from the group consisting of cholera toxin B (CTB), diphtheria toxin, tetanus toxoid, pertussis toxin, pertussis filamentous hemagglutinin, shiga toxin, ricin B 30 subunit, abrin, sweet pea lectin, retrovirus nucleoprotein (retro NP), rabies ribonucleoprotein (rabies RNP), Tobacco Mosaic Virus (TMV), cow pea mosaic virus, cauliflower mosaic virus, vesicular stomatitis virus-nucleocapsid protein (VSV-N), recombinant pox virus subunits and vectors, Semliki forest virus vectors, 35 Pseudomonas endotoxin, multiantigenic peptides (MAP), yeast virus-
- like particles (VPLs), malarial protein antigen, and microspheres.

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7. The conjugate of claim 6 wherein the T cell epitope-containing carrier comprises cholera toxin B (CTB).

- 8. The conjugate of claim 6 wherein said T cell epitope containing carrier is selected from the group consisting of cholera toxin B (CTB), retrovirus nucleoprotein (retro NP), rabies ribonucleoprotein (rabies RNP) vesicular stomatitis virusnucleocapsid protein (VSV-N), recombinant small pox virus subunit and vectors, and multiantigenic peptides (MAP).
- 9. The conjugate of claim 8 wherein MAP comprises a defined T cell epitope-containing peptide which is further conjugated to a multi-haptenated lysine branch structure at the amino terminus end of the peptide.
 - 10. A hapten-carrier conjugate selected from the group consisting of PS-2, PS-4, PS-5, and PS-6.
 - 11. The hapten-carrier conjugate of claim 10 wherein at least one hapten is coupled to the carrier.
- 12. The hapten-carrier conjugate of claim 11 wherein at least two haptens are coupled to the carrier, and the haptens are the same.
 - 13. The hapten-carrier conjugate of claim 11 wherein the carrier is multivalent.
- 30 14. The conjugate of claim 10 comprising PS-5.
 - 15. A therapeutic composition comprising at least one conjugate of claim 1 and a pharmacologically acceptable excipient.
- 35 16. A therapeutic composition comprising at least one conjugate of claim 6 and a pharmaceutically acceptable carrier.





- 17. The therapeutic composition of claim 16 further comprising an adjuvant.
- 18. The therapeutic composition of claim 17 wherein the adjuvant is alum, MF59 or RIBI adjuvant.
- 19. The therapeutic composition of claim 16 wherein the composition is soluble in an aqueous solution at a physiologically acceptable pH.
 - 20. The therapeutic composition of claim 16 wherein the composition is in suspension in an aqueous solution at a physiologically acceptable pH.
 - 21. A method of treating drug addiction to cocaine in mammals comprising:
 - (a) administering a therapeutically effective amount of the therapeutic composition
 - of claim 8 to a subject mammal; and

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- (b) monitoring the mammal for a desired therapeutic effect, wherein an increase of anti-drug antibodies is an indication of the desired therapeutic effect.
- 25 22. A method of treating drug addiction to cocaine in mammals comprising:
 - (a) administering a therapeutically effective amount of the therapeutic composition of claim 10 to a subject mammal; and
 - (b) monitoring the subject mammal for a desired therapeutic effect, wherein an increase of anti-drug antibodies is an indication of the desired therapeutic effect.
- 23. A method of treating drug addiction to cocaine in mammals comprising administering a therapeutically effective amount of the therapeutic composition of claim 16 to a mammal in need of treatment for drug addiction.



- 24. A method of treating drug addiction to cocaine in mammals comprising administering a therapeutically effective amount of a composition of claim 17 to a mammal in need of treatment for drug addiction.
- 25. A modified hapten having the structure shown in Figure 1b, wherein A, B, C, D, E, and F are each selected from the group of chemical moieties identified by CJ reference number, consisting of:

15	CJ 0	Q
	CJ 1	(CH ₂) _n Q
	CJ 1.1	co ₂ Q
	CJ 1.2	COQ
20	CJ 1.3	och ₃
	СЈ 2	OCO (CH ₂) Q
	CJ 2.1	OCOCH=Q
	CJ 2.2	ососн (о) сн ₂
	CJ 2.3	(-)
	CJ 3	CO(CH ₂) COQ
25	СЈ 3.1	
	CJ 4	oco(CH ₂) COQ
	CJ 4.1	OCO (CH ₂) CNQ
	CJ 5	CH ₂ OCO (CH ₂) COQ
30	CJ 5.1	CH2OCO (CH2) CNQ
	CJ 6	CONH (CH ₂) Q
	сј 7	Y(CH ₂) _n Q
	СЈ 7.1	CH ₂ Y(CH ₂) _n Q
	CJ 8	ососн (он) сн ₂ Q
	CJ 8.1	OCO (CH ₂) CH (OH) CH ₂ Q
35	CJ 9	ococ ₆ H ₅
	CJ 10	. 01
	СЈ 11	YCO(CH ₂) nCOQ



wherein Y is sulfur (S), oxygen (O), or an amine (NH), n is an integer from 3 to 20, and Q is selected from the group consisting of: H, OH, OCH3, CH2, CH3, COOH, halogens, activated esters, mixed anhydrides, acyl halides, acyl azides, alkyl halides, N-maleimides, imino esters, isocyanate, and isothiocyanate; with the proviso that at least one of A, B, C, D, E, or F is capable of conjugation with a T cell epitope-containing carrier molecule.

26. The hapten of claim 25 wherein the activated ester is 2-nitro-4-sulfophenyl ester or N-oxysuccinimidyl ester.

- 27. A hapten-carrier conjugate wherein the hapten is a drug or drug derivative selected from the group consisting of hallucinogens, cannabinoids, stimulants, nicotine, depressants, opium, and synthetic opiates, and wherein the carrier is a T cell epitope-containing molecule, wherein the conjugate is capable of inducing production of an antibody having a greater affinity for pharmacologically active drug than for pharmacologically inactive drug metabolites.
- 28. The conjugate of claim 27 wherein the hapten is selected from
 25 the group consisting of LSD, THC, amphetamines, cocaine,
 phenmetrazine, methylphenidate, nicotine, methaqualone,
 barbiturates, diazepam, flurazepam, phencyclidine, fluoxetine,
 opium, heroin, methadone, morphine, meperidine, codeine,
 pentazocine, propoxyphene and derivatives thereof.

29. The conjugate of claim 27 wherein the hapten is selected from the group consisting of amphetamines, cocaine, nicotine, heroin, and diazepam.

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- 30. The conjugate of claim 27 wherein the drug derivative is a drug modified to facilitate conjugation with a T cell epitope-containing carrier, but is sufficiently similar to the drug so as to elicit anti-drug antibodies specific for the drug.
- 31. A method for treating drug addiction in a mammal comprising administering to an affected mammal an antibody specific for the hapten-carrier conjugate of claim 1.
- 32. The method of claim 31 wherein the antibody is selected from the group consisting of a polyclonal antibody and a monoclonal antibody.
- 33. The method of claim 31 wherein the antibody is specific for the hapten portion of the conjugate of claim 1.
- 34. A method for treating drug addiction in a mammal comprising administering to an affected mammal an antibody specific for the hapten component of the hapten-carrier conjugate of claim 1, and the hapten-carrier conjugate of claim 1.
- 35. A method for treating drug addiction in a mammal comprising administering to an affected mammal an antibody specific for the hapten component of the hapten-carrier conjugate of claim 10.
 - 36. A process for the preparation of a PS-5 conjugate comprising the steps of:
 - a) reacting a solution of norcocaine hydrochloride and triethylamine in methylene chloride with succinic anhydride to form a mixture of solvents and product;
 - b) purifying the product from the mixture;
 - c) mixing the product with DMF, DIEA, and an activating agent to form a first solution;

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- d) adding dropwise the first solution to a second solution to form a conjugate mixture, the second solution comprising a carrier and a buffer in a selected pH range; and
- e) purifying the conjugate from the conjugate mixture.
- 37. A process for the preparation of a PS-5 conjugate comprising the steps of:
 - a) reacting a carrier with succinic anhydride in borate buffer and 1,4-dioxane to form a carrier solution maintained at a pH in a selected range;
 - b) dialyzing the solution against aqueous triethylamine;

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- c) lyophilizing the dialyzed solution to form succinylated carrier;
- d) diluting the succinylated carrier with buffer to form a buffered solution;
- e) treating the buffered solution with EDC and then norcocaine hydrochloride to form a conjugate solution; and
- f) purifying the conjugate from the conjugate solution.
- 38. A process for preparing a cocaine derivative useful in preparing a drug-carrier conjugate, the process comprising combining a radical 2 and general compound 1 of Figure 15 at low temperature, resulting in cyclization to form the 3β -benzoate ester adduct 4, as shown in Figure 15.
 - 40. An antibody produced in response to the conjugate of claim 1.
 - 41. The antibody of claim 40 selected from the group consisting of a polyclonal antibody and a monoclonal antibody.
 - 42. The antibody of claim 40 which is specific for the hapten portion of the conjugate of claim 1.
 - 43. A hapten-carrier conjugate comprising the structure shown in Figure 17b, wherein A, B, C, D, E and F are branches off a nicotine molecule, and are each selected from the group of





chemical moieties identified by CJ reference number, consisting of:

•	CJ 0	Q
5		(CH ₂) Q
	CJ 1.1	
	CJ 1.2	COQ
10	СЈ 1.3	OCH
		oco (сн ₂) nQ
	CJ 2.1	OCOCH=Q .
	CJ 2.2	OCOCH (O) CH ₂
	СЈ 2.3	
	CJ 3	
15	CJ 3.1	CO(CH ₂) CNQ
	CJ 4	OCO(CH ₂) COQ
		OCO(CH ₂) CNQ
	CJ 5	CH ₂ OCO (CH ₂) COQ
	CJ 5.1	$CH_2OCO(CH_2)$ CNQ
20	CJ 6	CONH (CH ₂) Q
	СЈ 7	$Y(CH_2)_nQ$
	CJ 7.1	CH ₂ Y(CH ₂) _n Q
	CJ 8	
25	CJ 8.1	OCO (CH ₂) CH (OH) CH ₂ Q
	CJ 9	ococ ₆ H ₅
	СЈ 10	See Figure 2b
	CJ 11	YCO(CH ₂) COQ

wherein Y is sulfur (S), oxygen (O), or an amine (NH), wherein n
is an integer from 3 to 20, and wherein Q is selected from the
group consisting of: H, OH, OCH3, CH2, CH3, COOH, halogens,
activated esters, mixed anhydrides, acyl halides, acyl azides,
alkyl halides, N-maleimides, imino esters, isocyanate,
isothiocyanate, and a T cell epitope-containing carriers; with
the proviso that Q in at least one of A, B, C, D, E, or F
comprises at least one T cell epitope containing carrier, and the





conjugate, with the exception of the T cell epitope-containing carrier, is referred to herein as the hapten.

- 44. The hapten-carrier conjugate of claim 43 wherein at least one hapten is coupled to the carrier.
 - 45. The hapten-carrier conjugate of claim 44 wherein at least two haptens are coupled to the carrier, and the haptens are the same.
- 10 46. The hapten-carrier conjugate of claim 44 wherein the carrier is multivalent.
- 47. The conjugate of claim 43 wherein the T cell epitopecontaining carrier is selected from the group consisting of a T
 cell epitope-containing protein, a modified T cell epitopecontaining protein, a T cell epitope-containing peptide, a
 modified T cell epitope-containing peptide, a T cell epitopecontaining peptidomimetic, T cell epitope-containing
 multiantigenic peptides (MAP), and at least one of the chemical
 moieties being identified by the CJ reference number and
 comprising at least one T cell epitope.
- 48. The conjugate of claim 47 wherein the T cell epitopecontaining carrier is selected from the group consisting of

 25 cholera toxin B (CTB), diphtheria toxin, tetanus toxoid, pertussis
 toxin, pertussis filamentous hemagglutinin, shiga toxin, ricin B
 subunit, abrin, sweet pea lectin, retrovirus nucleoprotein (retro
 NP), rabies ribonucleoprotein (rabies RNP), Tobacco Mosaic Virus
 (TMV), cow pea mosaic virus, cauliflower mosaic virus, vesicular

 30 stomatitis virus-nucleocapsid protein (VSV-N), recombinant pox
 virus subunits and vectors, Semliki forest virus vectors,
 Pseudomonas endotoxin, multiantigenic peptides (MAP), yeast viruslike particles (VPLs), malarial protein antigen, and microspheres.





conjugate, with the exception of the T cell epitope-containing carrier, is referred to herein as the hapten.

- 44. The hapten-carrier conjugate of claim 43 wherein at least one hapten is coupled to the carrier.
 - 45. The hapten-carrier conjugate of claim 44 wherein at least two haptens are coupled to the carrier, and the haptens are the same.
- 10 46. The hapten-carrier conjugate of claim 44 wherein the carrier is multivalent.
- 47. The conjugate of claim 43 wherein the T cell epitopecontaining carrier is selected from the group consisting of a T
 cell epitope-containing protein, a modified T cell epitopecontaining protein, a T cell epitope-containing peptide, a
 modified T cell epitope-containing peptide, a T cell epitopecontaining peptidomimetic, T cell epitope-containing
 multiantigenic peptides (MAP), and at least one of the chemical
 moieties being identified by the CJ reference number and
 comprising at least one T cell epitope.
- 48. The conjugate of claim 47 wherein the T cell epitopecontaining carrier is selected from the group consisting of

 25 cholera toxin B (CTB), diphtheria toxin, tetanus toxoid, pertussis
 toxin, pertussis filamentous hemagglutinin, shiga toxin, ricin B
 subunit, abrin, sweet pea lectin, retrovirus nucleoprotein (retro
 NP), rabies ribonucleoprotein (rabies RNP), Tobacco Mosaic Virus
 (TMV), cow pea mosaic virus, cauliflower mosaic virus, vesicular

 30 stomatitis virus-nucleocapsid protein (VSV-N), recombinant pox
 virus subunits and vectors, Semliki forest virus vectors,
 Pseudomonas endotoxin, multiantigenic peptides (MAP), yeast viruslike particles (VPLs), malarial protein antigen, and microspheres.





- 49. The conjugate of claim 48 wherein the T cell epitope-containing carrier comprises cholera toxin B (CTB).
- 5 50. The conjugate of claim 48 wherein said T cell epitope containing carrier is selected from the group consisting of cholera toxin B (CTB), retrovirus nucleoprotein (retro NP), rabies ribonucleoprotein (rabies RNP) vesicular stomatitis virus-nucleocapsid protein (VSV-N), recombinant small pox virus subunit and vectors, and multiantigenic peptides (MAP).
- 51. The conjugate of claim 50 wherein MAP comprises a defined T cell epitope-containing peptide which is further conjugated to a multi-haptenated lysine branch structure at the amino terminus end of the peptide.
 - 52. A hapten-carrier conjugate selected from the group consisting of PS-51, PS-52, PS-53, and PS-54 as depicted in Figure 18.
- 53. The hapten-carrier conjugate of claim 52 wherein at least one hapten is coupled to the carrier.
 - 54. The hapten-carrier conjugate of claim 52 wherein at least two haptens are coupled to the carrier, and the haptens are the same.
 - 55. The hapten-carrier conjugate of claim 53 wherein the carrier is multivalent.
- 56. A therapeutic composition comprising at least one conjugate of claim 43 and a pharmacologically acceptable excipient.
 - 57. A therapeutic composition comprising at least one conjugate of claim 48 and a pharmaceutically acceptable carrier.



- 58. The therapeutic composition of claim 57 further comprising an adjuvant.
- 59. The therapeutic composition of claim 58 wherein the adjuvant is alum, MF59 or RIBI adjuvant.
 - 60. The therapeutic composition of claim 57 wherein the composition is soluble in an aqueous solution at a physiological acceptable pH.
- 61. A method of treating drug addiction to nicotine in mammals comprising:

- (a) administering a therapeutically effective amount of the therapeutic composition of claim 50 to a subject mammal; and
- (b) monitoring the mammal for a desired therapeutic effect, wherein an increase of anti-drug antibodies is an indication of the desired therapeutic effect.
- 62. A method of treating drug addiction to nicotine in mammals comprising:
 - (a) administering a therapeutically effective amount of the therapeutic composition of claim 52 to a subject mammal; and
 - (b) monitoring the subject mammal for a desired therapeutic effect, wherein an increase of anti-drug antibodies is an indication of the desired therapeutic effect.
- 63. A method of treating drug addiction to nicotine in mammals comprising administering a therapeutically effective amount of the therapeutic composition of claim 57 to a mammal in need of treatment for drug addiction.
- 64. A method of treating drug addiction to cocaine in mammals comprising administering a therapeutically effective amount of a composition of claim 58 to a mammal in need of treatment for drug addiction.





65. A modified hapten having the structure shown in Figure 17b, wherein A, B, C, D, E and F are each selected from the group of chemical moieties identified by CJ reference number, consisting of:

	CJ 0	Q
10	CJ 1	(CH ₂) DQ
	СЈ 1.1	-
	CJ 1.2	COQ .
	CJ 1.3	OCH ₃
	CJ 2	OCO (CH ₂) Q
	CJ 2.1	OCOCH=Q
	CJ 2.2	OCOCH (O) CH ₂
	CJ 2.3	$OCO(CH_2)$ CH OCH_2
	CJ 3	CO(CH ₂) COQ
20		CO(CH ₂) CNQ
	CJ 4	oco(cH ₂) coQ
	CJ 4.1	$OCO(CH_2)$ CNQ
	CJ 5	$CH_2OCO(CH_2)_nCOQ$
25	CJ 5.1	$CH_2OCO(CH_2)_nCNQ$
	CJ 6	CONH (CH ₂) nQ
	СЈ 7	Y(CH ₂) _n Q
	CJ 7.1	CH ₂ Y(CH ₂) _n Q
	CJ 8	OCOCH (OH) CH ₂ Q
	CJ 8.1	$OCO(CH_2)$ CH $OH)CH_2Q$
	, Cl 8	ococ ₆ ^H ₅
	CJ 10	See Figure 2b
30	CJ 11	YCO(CH ₂) COQ

wherein Y is sulfur (S), oxygen (O), or an amine (NH), n is an integer from 3 to 20, and Q is selected from the group consisting of: H, OH, OCH3, CH2, CH3, COOH, halogens, activated esters, mixed anhydrides, acyl halides, acyl azides, alkyl halides, N-maleimides, imino esters, isocyanate, and isothiocyanate; with



the proviso that at least one of A, B, C, D, E, or F is capable of conjugation with a T cell epitope-containing carrier molecule.

- 66. The hapten of claim 65 wherein the activated ester is 2-5 nitro-4-sulfophenyl ester or N-oxysuccinimidyl ester.
- 67. A method for treating drug addiction in a mammal comprising administering to an affected mammal an antibody specific for the hapten-carrier conjugate of claim 43.
 - 68. The method of claim 67 wherein said antibody is selected from the group consisting of a polyclonal antibody and a monoclonal antibody.
 - 69. The method of claim 67 wherein the antibody is specific for the hapten portion of the conjugate of claim 43.

- 70. A method for treating drug addiction in a mammal comprising administering to an affected mammal an antibody specific for the hapten component of the hapten-carrier conjugate of claim 52.
- 71. An antibody produced in response to the conjugate of claim 25 43.
 - 72. The antibody of claim 71 selected from the group consisting of a polyclonal antibody and a monoclonal antibody.
- 73. The antibody of claim 71 which is specific for the hapten portion of the conjugate of claim 43.
- 74. The therapeutic composition of claim 57 wherein the composition is in suspension in an aqueous solution at a physiologically acceptable pH.



- 75. A method of preventing addiction to a drug in a mammal, said method comprising:
- (a) administering an effective amount of the conjugate of claim 9 to said mammal;
- (b) monitoring the mammal for a desired preventative effect, wherein production of anti-drug antibodies is an indication of the desired preventative effect.
- 76. A method of preventing addiction to a drug in a mammal, said method comprising:
 - (a) administering an effective amount of the therapeutic composition of claim 16 to said mammal;
- (b) monitoring the mammal for a desired preventative effect, wherein production of anti-drug antibodies is an indication of the desired preventative effect.
 - 77. A method of preventing addiction to a drug in a mammal, said method comprising:
- (a) administering an effective amount of the conjugate of20 claim 49 to said mammal;
 - (b) monitoring the mammal for a desired preventative effect, wherein production of anti-drug antibodies is an indication of the desired preventative effect.
- 78. A method of preventing addiction to a drug in a mammal, said method comprising:
 - (a) administering an effective amount of the therapeutic composition of claim 57 to said mammal;
- (b) monitoring the mammal for a desired preventative effect,
 wherein production of anti-drug antibodies is an indication of the desired preventative effect.
 - 79. The method according to claim 21 wherein the administration is enteral or parenteral.





- 80. The method according to claim 79 wherein the administration is oral or intramuscular.
- 81. The method according to claim 61 wherein the administration is enteral or parenteral.
 - 82. The method according to claim 81 wherein the administration is oral or intramuscular.
- 10 83. Succinylated norcocaine.
- 84. A process for the preparation of succinylated norcocaine comprising the step of reacting a solution of norcocaine hydrochloride and triethylamine in methylene chloride with succinic anhydride to form succinylated norcocaine.
 - 85. Succinylated norcocaine obtained from the process according to claim 84.
- 20 86. A process for the preparation of succinylated norcocaine comprising the step of reacting a solution of norcocaine monoactivated succinic acid and triethylamine to form succinylated norcocaine.
- 25 87. Succinylated norcocaine obtained from the process according to claim 84.